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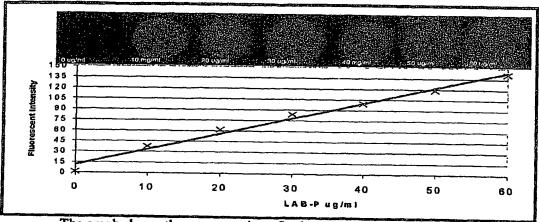
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(54) Title: CELL TARGETING METHODS AND COMPOSITIONS



The graph shows the concentration of palmitated protein G (or lipidated antibody binding protein [LAB-P]) on the x-axis and the relative fluorescent intensity in arbitrary units on the y-axis. The insert shows fluorescent micrographs of representative cells coated with PPG at the indicated concentrations.

(57) Abstract: In certain aspects, the invention relates to cell delivery compositions comprising a progenitor cell and a targeting moiety, and methods related thereto. Such compositions and methods may be used, for example, in administering a targeted cell therapy to a subject.

Int anal Application No PC I / US2004/008763

PC1/US2004/008763 A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C12N5/00 C12N C12N5/06 A61K45/00 According to international Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) IPC 7 C12N A61K Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the International search (name of data base and, where practical, search terms used) EPO-Internal, BIOSIS C. DOCUMENTS CONSIDERED TO BE RELEVANT Category ° Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. P,X WO 03/106640 A (COHEN NIR ; UNIV CASE 1-7, 11-14, WESTERN RESERVE (US); CAPLAN ARNOLD I (US); DENN) 24 December 2003 (2003-12-24) 26,27, 29-33. 35,37, 39,40 the whole document Y CAPLAN A I ET AL: "MESENCHYMAL STEM 1-42 CELLS: BUILDING BLOCKS FOR MOLECULAR MEDICINE IN THE 21ST CENTURY" TRENDS IN MOLECULAR MEDICINE, XX, XX, vol. 7, no. 6, June 2001 (2001-06), pages 259-264, XP001156351 page 262, left-hand column -/--Further documents are listed in the continuation of box C. X Patent family members are listed in annex. Special categories of cited documents: \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docu-ments, such combination being obvious to a person skilled in the art. "O" document referring to an oral disclosure, use, exhibition or \*P\* document published prior to the international filing date but later than the priority date claimed \*&\* document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 3 September 2004 10/11/2004 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nt, Fax: (+31-70) 340-3016 Vogt, T

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Ó (O: 41)		PC1/US2004/008763
	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Υ	WO 00/23570 A (BISYS B V U) 27 April 2000 (2000-04-27) the whole document	1-42
A	KIM S A ET AL: "THE USE OF PALMITATE—CONJUGATED PROTEIN A FOR COATING CELLS WITH ARTIFICIAL RECEPTORS WHICH FACILITATE INTERCELLULAR INTERACTIONS" JOURNAL OF IMMUNOLOGICAL METHODS, ELSEVIER SCIENCE PUBLISHERS B.V., AMSTERDAM, NL, vol. 158, 1993, pages 57-65, XP002940258 ISSN: 0022-1759 the whole document	
P,A	WO 03/072542 A (MIDDLETON CRYSTAN; WALSH ELISABETH B (US); UNIV DUKE (US); KENAN DANI) 4 September 2003 (2003-09-04) the whole document	
P,A	US 2003/149235 A1 (BAKER ANDREW HOWARD ET AL) 7 August 2003 (2003-08-07) the whole document	
A	WO 02/090985 A (MIHARA HISAKAZU ; NOKIHARA KIYOSHI (JP)) 14 November 2002 (2002-11-14) the whole document	
A	WO 03/009881 A (IMARX THERAPEUTICS INC) 6 February 2003 (2003-02-06) the whole document	
A	WO 02/20722 A (PASQUALINI RENATA; ARAP WADIH (US); UNIV TEXAS (US)) 14 March 2002 (2002-03-14) the whole document	
A	WO 01/92549 A (ROELVINK PETRUS W ; EINFELD DAVID (US); GENVEC INC (US); KOVESDI IMRE) 6 December 2001 (2001-12-06) the whole document	
Ą	WO 99/46284 A (BURNHAM INST) 16 September 1999 (1999-09-16) the whole document	
A	WO 98/53804 A (SAMOILOVA TATIANA ; SMITH BRUCE F (US); UNIV AUBURN (US)) 3 December 1998 (1998-12-03) the whole document	
	<b>-/</b>	

int lal Application No PCT/US2004/008763

A TREPEL MARTIN ET AL: "Molecular adaptors for vascular-targeted adenoviral gene delivery" HUMAN GENE THERAPY, vol. 11, no. 14, 20 September 2001 (2001-09-20), pages 1971-1981, XP001182897 ISSN: 1043-0342 the whole document  A SAMOYLOV A M ET AL: "Recognition of cell-specific binding of phage display derived peptides using an acoustic wave sensor" BIOMOLECULAR ENGINEERING, ELSEVIER, NEW YORK, NY, US, vol. 18, no. 6, February 2002 (2002-02), pages 269-272, XP004336425 ISSN: 1389-0344 the whole document  A AKERMAN MARIA E ET AL: "Nanocrystal targeting in vivo" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, vol. 99, no. 20, 1 October 2002 (2002-10-01), pages 15SN: 0027-8424 the whole document
TREPEL MARTIN ET AL: "Molecular adaptors for vascular-targeted adenoviral gene delivery" HUMAN GENE THERAPY, vol. 11, no. 14, 20 September 2001 (2001-09-20), pages 1971-1981, XP001182897 ISSN: 1043-0342 the whole document  A SAMOYLOV A M ET AL: "Recognition of cell-specific binding of phage display derived peptides using an acoustic wave sensor" BIOMOLECULAR ENGINEERING, ELSEVIER, NEW YORK, NY, US, vol. 18, no. 6, February 2002 (2002-02), pages 269-272, XP004336425 ISSN: 1389-0344 the whole document  A KERMAN MARIA E ET AL: "Nanocrystal targeting in vivo" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, vol. 99, no. 20, 1 October 2002 (2002-10-01), pages 12617-12621, XP001182896 ISSN: 0027-8424
for vascular-targeted adenoviral gene delivery" HUMAN GENE THERAPY, vol. 11, no. 14, 20 September 2001 (2001-09-20), pages 1971-1981, XP001182897 ISSN: 1043-0342 the whole document  A SAMOYLOV A M ET AL: "Recognition of cell-specific binding of phage display derived peptides using an acoustic wave sensor" BIOMOLECULAR ENGINEERING, ELSEVIER, NEW YORK, NY, US, vol. 18, no. 6, February 2002 (2002-02), pages 269-272, XP004336425 ISSN: 1389-0344 the whole document  A KKERMAN MARIA E ET AL: "Nanocrystal targeting in vivo" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, vol. 99, no. 20, 1 October 2002 (2002-10-01), pages 12617-12621, XP001182896 ISSN: 0027-8424
cell-specific binding of phage display derived peptides using an acoustic wave sensor" BIOMOLECULAR ENGINEERING, ELSEVIER, NEW YORK, NY, US, vol. 18, no. 6, February 2002 (2002-02), pages 269-272, XP004336425 ISSN: 1389-0344 the whole document  AKERMAN MARIA E ET AL: "Nanocrystal targeting in vivo" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, vol. 99, no. 20, 1 October 2002 (2002-10-01), pages 12617-12621, XP001182896 ISSN: 0027-8424
targeting in vivo" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, vol. 99, no. 20, 1 October 2002 (2002-10-01), pages 12617-12621, XP001182896 ISSN: 0027-8424

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Roy II Observations where certain claims were found we seemble (Centinus in a Charles of the continue i
Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X Claims Nos.: 43–89, 90–95, 142–189 because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
Claims Nos.:     because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful international Search can be carried out, specifically:
3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
· :
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this international Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this international Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark on Protest The additional search fees were accompanied by the applicant's protest.
No protest accompanied the payment of additional search fees.

# FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Claims Nos.: 43-89, 90-95, 142-189

Claims 43-89 relate to a method of delivering a progenitor cell, comprising administrating said progenitor cell to a subject. Claims 90-95 relate to a method of treating a disease, comprising delivering the progenitor cell to a target tissue. Claims 142-189 relate to a method of delivering a scaffold graft in a target tissue, comprising implanting said scaffold graft. Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy.

Int: nal Application No PC:/uS2004/008763

						7C1/US2	004/008763
cite	Patent document ad in search report		Publication date		Patent family member(s)		Publication date
WO	03106640	Α	24-12-2003	WO US	03106640 2004048370	A2 A1	24-12-2003 11-03-2004
WO	0023570	Α	27-04-2000	CA	2348153	 A1	27-04-2000
				EP	1001017	A1	17-05-2000
				JP	2002527103	T	27~08-2002
				WO	0023570		27-04-2000
				NZ	511695		26-09-2003
				US	2003161813	A1	28-08-2003
				US	6440736	B1	27-08-2002
WO	03072542	Α	04-09-2003	CA	2467836		04-09-2003
				MO	03072542	A2	04-09-2003
				US 	2003185870	A1	02-10-2003
US —	2003149235	A1	07-08-2003	NONE		ر بے رک سندے سے ۔۔۔	
WO	02090985	Α	14-11-2002	EP	1403640	A1	31-03-2004
			_	WO	02090985		14-11-2002
WO	03009881		06-02-2003	US	2002041898	Δ1	11-04-2002
	, <del></del>		JJ JL 2000	MO	03009881		06-02-2003
				US	2004009229		15-01-2004
ΜO	0220722	Α	14-03-2002	AU	8884301		22-03-2002
				AU	8891401		22-03-2002
				AU	9065201		22-03-2002
				ΑU	9066201		22-03-2002
				ΑU	9066301		22-03-2002
				CA	2421191	A1	14-03-2002
				CA	2421195		14-03-2002
				CA	2421200		14-03-2002
				CA	2421271		14-03-2002
				CA	2421380		14-03-2002
				ΕP	1322755		02-07-2003
				EP	1315840		04-06-2003
				EP	1315965		04-06-2003
				EP	1315830		04-06-2003
				EP	1315512		04-06-2003
				JP	2004515751		27-05-2004
				JP WO	2004508045	-	18-03-2004
				WO WO	0220769 0220722		14-03-2002
				WO	0220723		14-03-2002
				MO	0220723		14-03-2002
					ULLU/24		14-03-2002
				WO	0220822	A2	14-03-2002
 WO	 0192549		 06-12-2001	WO			
 WO	0192549	 А	06-12-2001	₩0 	6515401	 A	11-12-2001
 WO	0192549	 А	 06-12-2001	WO AU EP	6515401 1301612	 A A2	11-12-2001 16-04-2003
 WO	0192549	Α	 06-12-2001	₩0 	6515401 1301612 2003534806	 A A2 T	11-12-2001 16-04-2003 25-11-2003
WO	0192549	A	 06-12-2001	WO AU EP JP	6515401 1301612	 A A2 T A2	11-12-2001 16-04-2003
	0192549 9946284	A A	06-12-2001	WO AU EP JP WO	6515401 1301612 2003534806 0192549 2003099619	A A2 T A2 A1	11-12-2001 16-04-2003 25-11-2003 06-12-2001 29-05-2003
				AU EP JP WO US	6515401 1301612 2003534806 0192549 2003099619	A A2 T A2 A1 B1	11-12-2001 16-04-2003 25-11-2003 06-12-2001 29-05-2003
				AU EP JP WO US	6515401 1301612 2003534806 0192549 2003099619	A A2 T A2 A1  B1 B1	11-12-2001 16-04-2003 25-11-2003 06-12-2001 29-05-2003 
				AU EP JP WO US US	6515401 1301612 2003534806 0192549 2003099619 6232287 6174687	AA2 A2 A2 A2 A1  B1 B1 B2	11-12-2001 16-04-2003 25-11-2003 06-12-2001 29-05-2003

Int nal Application No
PCI/OS2004/008763

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
WO 9946284	A		EP JP WO US	1062232 A2 2002506079 T 9946284 A2 6610651 B1	27-12-2000 26-02-2002 16-09-1999 26-08-2003
WO 9853804	Α	03-12-1998	AU EP US WO US	7698698 A 1005330 A1 6329501 B1 9853804 A1 2002137023 A1	30-12-1998 07-06-2000 11-12-2001 03-12-1998 26-09-2002